REMARKS

Claims 1-10, 12, 35-37, and 39-52 are pending in the present application. Claim 12 has been amended in order to depend from claim 1 while new claims 43-52 have been added. Support for the new claims can be found, *inter alia*, on page 5 lines 23-24; page 6 lines 26-30; page 8 lines 4-5; and page 11 lines 23-34, of the specification. Accordingly, no new matter has been introduced into the application by the above-amendment.

Pursuant to Rule 607(c), applicants bring to the Examiner's attention the fact that claims 43 and 52 are believed to substantially correspond to claims 3 and 1, respectively, of U.S. patent 6,680,334.

Rejection over Lazar (and Davison)

Claims 1-10, 12, and 35-40 [sic][1] have been rejected under 35 U.S.C. § 103(a) over U.S. patent 5,155,120 (Lazar) and additionally in view of U.S. patent 4,879,303 (Davison). This rejection is respectfully traversed.

The present invention relates to the use of crystalline amlodipine free base. Surprisingly, crystalline amlodipine free base, especially crystalline Form I, is suitable for use in making a pharmaceutical composition such as a tablet. The prior art taught that amlodipine free base was undesirable, e.g. for excessive stickiness to tablet punches. See Davison at column 4 table 2.

Lazar generically teaches the use of amlodipine and its salts for treating congestive heart failure. Although the example in the patent refers to "amlodipine" as the active ingredient, column 3 lines 29-31 clarify that "the following example w[as] conducted with amlodipine benzenesulfonate." Thus, a composition containing amlodipine free base was not made or used in Lazar. Instead, Lazar followed the teachings of Davison and used amlodipine in the form of an amlodipine besylate.

Neither Lazar nor Davison teach the use of crystalline amlodipine free base, and certainly neither patent teaches crystalline Form I or Form II amlodipine free base. The applied prior art fails to suggest the claimed invention. And in fact the applied prior art

[1] Claim 38 was cancelled prior to the final office action and new claims 41 and 42 were added. Applicants assume that the Examiner's rejection applied to all pending claims.

teaches away from the presently claimed invention, directing the use of amlodipine benzenesulfonate. The rejection thus fails to establish a prima facie case of obviousness.

The Examiner previously considered such distinctions but suggested that applicants provide a showing of the differences between crystalline forms and amorphous forms. Accordingly, to expedite prosecution, applicants submit herewith the Rule 132 Declaration of Arlette Vanderheijden (executed version to follow shortly). In the Declaration, four amlodipine free base substances were made and compared. Three were crystalline forms and the fourth was an amorphous form. While the four substances were going to be used to test for stickiness to tablet punches as described in Davison, it was impossible to make the amorphous amlodipine free base material into a tablettable composition. See ¶ 8 and Appendix B of the Declaration. The amorphous amlodipine free base was very sticky and could not be blended. As seen in Appendix B, the amorphous free base tends to form big lumps coated with a limited amount of the required excipient. A blended mixture of the tablet formulation (excipient plus free base) was not possible to be formed because of the physical properties of the amorphous amlodipine free base. Thus, the three crystalline forms were tested and measured for stickiness while the amorphous form was so unsuitable that the tabletting test could not be performed. See ¶¶ 10 and 12 of the Declaration. Accordingly, the form of the amlodipine free base does have a significant effect on the pharmaceutical composition.

Lazar and Davison do not teach or suggest that crystalline amlodipine free base would be superior or that crystalline Form I in particular would be advantageous. Thus, the claimed invention is unobvious within the meaning of 35 U.S.C. § 103.

Furthermore, the patentability of the present claims is also demonstrated by the teachings in U.S. 6,680,334 (Bentham). As recognized by Ms. Vanderheijden, Bentham indicates that Pfizer, the originator of amlodipine and the apparent owner of both Lazar and Davison, did not have a crystalline amlodipine free base until very recently. Having a partly amorphous amlodipine free base substance would explain the previously reported stickiness problem with amlodipine free base. Thus it is reasonable to conclude that the amlodipine free base mentioned in Lazar and Davison would have been at least partly

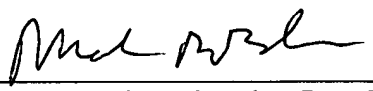
amorphous. See ¶ 12 of the Declaration. Thus, the applicants' claimed crystalline amlodipine free base is patentable over the applied prior art.

Finally, applicants point out that while Bentham claims crystalline amlodipine free base (see claim 1) and a pharmaceutical composition containing the same (see claim 3), Bentham is not prior art against the instant application. The priority of the present application goes back to December 29, 2000 whereas Bentham was first filed in the U.S. in October 2001. In as much as the USPTO has found the claims of Bentham to be patentable, the instant claims, with an earlier date of invention, must also be viewed as patentable by the USPTO.

In view of the above arguments, the enclosed Declaration and the data in the present application, including Example 9, the presently claimed subject matter is novel and unobvious over the applied prior art. Reconsideration and withdrawal of the rejection and allowance of the present application are respectfully requested.

Should the Examiner have any questions regarding this application, she is encouraged to contact Mark R. Buscher (Reg. No. 35,006) at telephone No. 703 753 5256.

Respectfully submitted,



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